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EXAMINER

SULLIVAN, DANIEL M

ART UNIT

PAPER NUMBER

1636

DATE MAILED: 04/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/879,329

Applicant(s)

SIGNER ET AL.

Examiner

Daniel M Sullivan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 09 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 8,9,19 and 20 is/are allowed.
- 6) ☒ Claim(s) 1,4,6,10,12,14,15,17 and 18 is/are rejected.
- 7) ☒ Claim(s) 2,3,5,7,11,13 and 16 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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### **DETAILED ACTION**

This Non-Final Office Action is a reply to the Papers filed 9 January 2004 in response to the Non-Final Office Action mailed 10 September 2003. Claims 1-20 were considered in the 10 September Office Action. Claims 1, 18 and 20 were amended in the 9 January Paper. Claims 1-20 are pending and under consideration.

#### ***Oath/Declaration***

Objection to the Declaration is withdrawn in view of the filing of a signed Declaration.

#### ***Response to Amendment***

##### Claim Objections

Objection to claims 18 and 20 as containing minor informalities is withdrawn.

##### Claim Rejections - 35 USC § 112

Rejection of claims 1, 4-6, 8, 10, 12, 14, 15 and 17-20 under 35 U.S.C. 112, first paragraph, as lacking adequate written description is withdrawn. Applicant argues persuasively that the nature and advantage of the presently claimed invention does not hinge upon use of a particular negative selection marker. As the particulars of the negative selection marker are not critical to the functioning of the invention, the marker is adequately described by the examples provided in the specification.

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Claim 18 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant's response does not address these grounds for rejection.

Claim Rejections - 35 USC § 102

Rejection of claims 1 and 4 under 35 U.S.C. 102(e) as being anticipated by Selten *et al.* U.S. Patent No. 6,051,431 is withdrawn in view of the amendment of the claims such that the negative selectable marker must be different in kind from the positive selectable marker.

***New Grounds***

Claim Rejections - 35 USC § 102

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by Bauer *et al.* U.S. Patent No. 6,534,315.

Bauer *et al.* teaches a genetic construct comprising a positive selectable marker gene and a negative selectable marker gene, different in kind from the positive selectable marker, and direct repeats of a gene of interest that flank the positive and negative selectable marker genes (see especially the paragraph beginning at line 34 in column 3 and the paragraph bridging columns 3-4). With regard to the limitation of the substrate as "complementary to" the selectable marker, Applicant indicates that this relationship is described in paragraph 30 of the specification. Based on the description therein, the limitation is understood to encompass any

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medium or growth condition that provides for selection by the marker gene. In columns 8-10, Bauer *et al.* contemplates a variety of positive and negative selectable marker genes and media or growth conditions that provide for selection (*e.g.*, inducers of promoters operably linked to nucleic acids encoding toxic gene products for use as negative selectable markers). Thus, Bauer *et al.* teaches a genetic construct having all of the limitations of the construct of the instant claim 1.

In the paragraph bridging columns 10-11, Bauer *et al.* teaches a method of removing a selectable marker comprising transforming cells with the genetic construct disclosed therein, identifying transformants using the integration marker (*i.e.*, positive selection marker) and then selecting cells that have lost the negative selection marker by culturing in negative selection medium. Thus, Bauer *et al.* teaches a method comprising the steps of the method of claim 4.

The genetic construct and method of Bauer *et al.* are the same as those claimed in the instant application; therefore, the claims are anticipated by Bauer *et al.*

#### Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 6, 10, 12, 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer *et al.* (*supra*).

The claims are directed to the genetic construct of claim 1, which is anticipated by the teachings of Bauer *et al.* (*Id.*), wherein the positive and negative selectable markers are limited to specific arrangement within the construct with respect to one another (*e.g.*, GI-PS-NS-GI *versus* GI-NS-PS-GI). Claims 14 and 15 are further limited to comprising additional genes of interest flanking the gene of interest present as a direct repeat. Although Bauer *et al.* does not explicitly teach any particular configuration of the positive and negative selectable markers, other than that they should be flanked by the direct repeat, the skilled artisan would not expect that the arrangement of the selectable markers within the boundaries of the direct repeat would affect the function of the construct in any way.

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A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities because one skilled in the art would be motivated by the expectation that compounds of similar structure will have similar function (see *e.g.*, MPEP 2144.09). Thus, it would be *prima facie* obvious to the skilled artisan to use either of the configurations of positive and negative selectable markers set forth in the claims. With regard to additional genes of interest, Bauer *et al.* teaches that the constructs might comprise one or several additional genes of interest located outside of the direct repeat sequence (see especially column 4, lines 11-14).

Given these teachings, the invention of claims 1, 6, 10, 12, 14 and 15, as a whole, would have been obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 4, 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bauer *et al.* as applied to claims 1 and 4 above and further in view of Ow, D. (WO 93/01283).

Bauer *et al.* teaches a method of removing a selectable marker comprising transforming cells with the genetic construct disclosed therein, identifying transformants using the integration marker and then selecting cells that have lost the negative selection marker by culturing in negative selection medium (*Id.*). Bauer *et al.* does not teach that the method can be applied to plants.

Ow teaches a method of producing marker-free transgenic plants wherein a selectable marker gene is flanked by site specific recombination sites and excised using a site specific recombinase (see especially the discussion beginning the first full paragraph on page 6 and continued through the first full paragraph on page 7).

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It would have been obvious to one of ordinary skill in the art to substitute the method of Bauer *et al.*, using a construct comprising a positive and negative selectable marker flanked by direct repeats according to the instant claims, for the method of Ow, which utilizes a selectable marker flanked by site specific recombination signals to remove selectable marker genes from plant cells. One would be motivated to modify the teachings of Ow in this way in view of the teaching of Bauer *et al.* that site specific recombination systems are inferior to the method disclosed therein because the site specific recombination does not remove all of the exogenous DNA (see especially column 3, lines 26-28).

Absent evidence to the contrary, one would have a reasonable expectation of success in practicing the method of Bauer *et al.* in plant cells because one of ordinary skill would expect that the homologous recombination required for deletion of the marker genes would operate in plant cells as well as yeast.

Finally, claim 18, which limits the cell of claim 17 to one of a variety of species, would also be obvious to one of ordinary skill in the art because Ow teaches that excision of marker genes is generally desirable in any transgenic plant (see especially the third paragraph on page 4) and explicitly contemplates production of marker-free tobacco (see especially Example 2).

For these reasons, the invention of claims 1, 4, 17 and 18 as a whole would be obvious to one of ordinary skill in the art at the time of filing.

#### ***Allowable Subject Matter***

Claims 2, 3, 5, 7, 11, 13 and 16 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of

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the base claim and any intervening claims. The art does not provide motivation to substitute the CodA marker gene for those contemplated therein.

Claims 8, 9, 19 and 20 are allowed. The art does not teach or suggest a method comprising the particular method steps set forth in claim 8.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

  
DAVID GUZO  
PRIMARY EXAMINER